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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
ARIANI, KADE	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Applicant argues that a prima facie case of obviousness has not been established, because Olsen does not disclose the presently claimed enzyme because Olsen discloses a subtilisin DY having a molecular weight of 27 kDa.

However, applicant seems to contradict their argument in their own specification (page 33 2nd paragraph) that " it was confirmed that the amino acid sequence of the purified enzyme obtained in Example 1 is completely identical to the subtilisin DY", and (page16 last paragraph) that "subtilisins may be used in the present invention, and subtilisin DY (WO/30682) is preferable". It must be noted that WO 98/30682 is the publication number of Olsen et al. Therefore, Olsen et al. teach the claimed enzyme, and since an enzyme cannot be separated from its properties, the properties, in this case, activity and substrate specificity, MW, pI, optimum pH, and optimum temperature, are necessarily present.

Moreover, a person of ordinary skill in the art at the time the invention was made would have known that during determination of molecular weight using SDS-PAGE, the molecular weight of a protein would depend on the percentage of the acrylamide gel used during the measurements, and since the mobility of the protein in the gel would depend on the percentage of the acrylamide gel used, thus molecular weight could vary from one experiment to another. Further support is based on the evidence in the specification (page 29, 2nd and 3rd paragraphs) that "an SDS-PAGE using a 12% gel ...and the molecular weight of the enzyme capable of digesting a pathogenic prion protein was approximately 31,000, ... another SDS-PAGE using a 15 % gel was carried out ... and the molecular weight of the enzyme capable of digesting a pathogenic prion

protein was approximately 26,000". Therefore, the molecular weight of an enzyme can change.

Applicant argues that the examiner has failed to provide reasons why one of skill in the art would combine the cited references to arrive at the claimed method of using the claimed enzyme.

However, Shih teaches a method for digesting of infectious prion proteins comprising the step of bringing the protein into contact with an enzyme, the enzyme is derived from *Bacillus licheniformis* (Abstract, Page 1 0002, 0006,0010, and Page 3 0054), wherein the contacting step is carried out without preheating the subject at 90ºC or more (page 2 0031). Shih teaches it will be recognized that any of a wide variety of proteases may be employed in the practice of the invention and that the choice of specific proteolytic enzyme will affect the choice of temperature that is used to carry the proteolytic degradation, as well as the choice of any elevate temperature treatment of the tissue before its exposure to the proteolytic enzyme (Page 3, 0046). Shih further teach the proteolytic enzymes that can be used include keratinase enzymes, subtilisins, and active fragments of a keratinase enzyme (Page 3 0053-0054). Shih teaches the method achieves a substantial advance in the art, permitting nutritional use of a material that would otherwise, in the absence of the treatment, constitute a biological hazard, and to avoid costs and infrastructure requirements for incineration and disposal of infected or contaminated animal tissue (page 4 0071). Shih further teaches a method for reduction of infective prion protein (a method for detoxifying a pathologic prion protein) (page 6 Claim 1). Shih teaches the enzyme is a serine protease (p.5 0086).

As mentioned immediately above, Olsen et al. teach subtilisin DY.

Therefore, a person of ordinary skill in the art at the time the invention was made could have been motivated to substitute the enzyme in the method as taught by Shih with the enzyme as taught by Olsen et al. to provide a method for digesting a protein highly resistant to denaturation and degradation and a method for detoxifying a pathologic prion protein with predictable results of digesting a protein highly resistant to denaturation and degradation and detoxifying a pathologic prion protein. Because substitution of one known proteolytic enzyme with another known proteolytic enzyme, in this case subtilisin DY, would have yielded predictable results to one of ordinary skill in the art at the time the invention was made. The motivation for using subtilisin DY as taught by Shih would be proteolytic enzymes including subtilisins could be used in the method of method for digesting of infectious prion proteins.

/Leon B Lankford/

Primary Examiner, Art Unit 1651